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10/539,527	07/10/2006	Jean-Philippe Girard	ENDOC.011APC	2903

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
04/29/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No.	Applicant(s)	
	10/539,527	GIRARD ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-26,28-37,58-71,125,127 and 128* is/are pending in the application.

4a) Of the above claim(s) *33-37,58-71,125 and 128* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-26,28-32 and 127* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6-17-2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of claims 23-26, 28-32 and 127 in the reply filed on March 6, 2008 is acknowledged. The traversal is on the ground(s) that all pending claims in the instant application form a unity of invention because the Merck manual does not teach the first claimed invention of ameliorating inflammation by modulating NF-HEV level of activity. This is found persuasive; however, the restriction requirement is still deemed proper because the instant application contains claims to different categories of invention under the meaning of 37 CFR 1.475(b)-(d), wherein CFR 1.475(b) states:

"An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn **only** to **one** of the following combinations of categories:

(1) A product and a process specially adapted for the manufacture of said product; or

(2) A product and process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the

said process.

37 CFR 1.475(c) states:

"If an application contains claims to more or less than one of the combination of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present."

37 CFR 1.475(d) also states:

"If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and 1.476(c)."

Since the instant application contains multiple processes (e.g., methods of ameliorating symptoms of a condition and methods of identifying a candidate inhibitor of an NF-HEV polypeptide), it is concluded that the present application lacks unity of invention.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

Currently, claims 23-26, 28-37, 58-71, 125, 127-128 are pending. Claims 33-37, 58-71, 125, and 128 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Accordingly, claims 23-26, 28-32, and 127 are under examination on the merits.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on June 17, 2005 is being considered by the examiner except citation numbers 2-8, which lack appropriate publication dates.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 recites "an antisense nucleic acid complementary to at least a portion of said NF-HEV polypeptide or a biologically active fragment thereof". See lines 3-4. Since an antisense nucleic acid comprises a nucleotide sequence, while a polypeptide comprises an amino acid sequence, it is unclear how an antisense nucleic acid comprising a nucleotide sequence can be complementary to an amino acid sequence, thereby rendering the claim indefinite. For examination purpose, the claim will be construed as "an antisense nucleic acid complementary to a nucleic acid encoding NF-HEV polypeptide or a biologically active fragment thereof".

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-26, 28-32, and 127 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The factors to be considered when analyzing claims for compliance with the written description requirement include: A) actual reduction to practice; B) disclosure of drawings or structural chemical formulas; C) sufficient relevant identifying characteristics; D) method of making the claimed invention; E) level of skill and knowledge in the art; and F) predictability in the art.

In the instant case, the claims are drawn to methods of ameliorating symptoms of an inflammatory condition by modulating the level of NF-HEV polypeptide by administrating a "compound", wherein the expression of a nucleic acid encoding NF-HEV polypeptide is reduced by an antisense nucleic acid. Hence, the "compound" and the "antisense nucleic acid" that result in the modulation of NF-HEV polypeptide in a subject, thereby ameliorating symptoms of an inflammatory condition are the critical elements for one of ordinary skill in the art to practice the claimed invention.

Although the specification provides a method of identifying and making NF-HEV inhibitors (see pages 37-42, 46, 50-54, 99-102, 109-111), such broad, generic, and prophetic description of a method for identifying and preparing a potential "compound" or "antisense

nucleic acid" is not predictive of making a therapeutic "compound" or "antisense nucleic acid" that confers a therapeutic efficacy of relieving an inflammatory symptoms in a subject as claimed in the instant case. The specification as originally filed does not provide any actual working example or embodiment comprising administering a compound or antisense nucleic acid that modulates NF-HEV activity and ameliorates an inflammatory condition, thereby failing to show that the inventors reduced the claimed invention to practice. Furthermore, there is no disclosure of drawings or structures for the claimed compound or antisense nucleic acid, thereby failing to describe sufficient relevant identifying characteristics (e.g., structure-function correlation, physical/chemical properties, complete structure, partial structure) for the claimed invention taken as a whole. Note that the specification does not disclose a representative number of species encompassed by the genus of compounds, and in fact, it fails to provide a structure (e.g., antisense nucleic acid sequence) of a single compound that would result in the amelioration of inflammatory symptoms by reducing NF-HEV activity, which is an essential element required by the claimed methods. See MPEP §2163, which teaches the following: "A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process." See also *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004), wherein the Court expressed that an adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. (emphasis added). The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the

PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described."

In view of the foregoing and the totality of the factors listed above, it is concluded that the mere disclosure of "how to obtain" a compound that may reduce NF-HEV activity and therefore may be capable of ameliorating symptoms of an inflammatory condition is not a sufficient description for the claimed methods administering a compound into a subject having symptoms of an inflammatory condition with a resultant effect of ameliorating said symptoms in said subject, and therefore, one of ordinary skill in the art would not recognize that the inventors were in possession of the genus of compounds, let alone the NF-HEV-specific antisense nucleic acid species, at the time of filing.

Claims 23-26, 28-30, 32, and 127 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of ameliorating symptoms of an inflammatory condition by inhibiting NF-HEV activity comprising administering an antisense nucleic acid, does not reasonably provide enablement for a method of ameliorating symptoms of an inflammatory condition by stimulating NF-HEV activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Claims 23-26 and 127 are drawn to a method of ameliorating symptoms of an inflammatory condition in a subject by "modulating" the level or activity of NF-HEV polypeptide. The word "modulating" embraces both stimulating and inhibiting as evidenced by the disclosure of the specification, which states "there is provided a method of modulating (e.g., stimulating or inhibiting)". See paragraph 0013. The specification also teaches that NF-HEV induces inflammatory responses while inhibition of NF-HEV reduces inflammatory responses. Consistent with the disclosure of the specification, the state of the prior art at the time of the invention was such that only inhibition of NF-HEV activity was known to be effective in treating or ameliorating symptoms of an inflammatory condition. See the prior art rejections applied in this Office action. Hence, "stimulating" the level or activity of NF-HEV, which is encompassed

by "modulating", would not result in the amelioration of symptoms of an inflammatory condition in a subject as required by the claims. In addition, the instant specification does not provide any working examples wherein an inhibitor of NF-HEV does indeed result in the amelioration of inflammatory symptoms in a subject having those symptoms. From the methods of identifying, preparing, and making the potential inhibitor to those of applying it for the intended therapeutic use, the disclosure of the specification is entirely prophetic and generic. In fact, there is not even a single *in vitro* working example wherein "inhibition" of NF-HEV in cultured cells results in inhibition of inflammatory responsive genes/proteins. The only working examples disclosed in the specification show "induction" or "overexpression" of NF-HEV in cultured cells also induce pro-inflammatory chemokines.

In addition, claims 23-26, 28-30, 32, and 127 are drawn to therapeutic methods which do not include any means of reducing the level of NF-HEV in a subject (e.g., administering or providing an inhibitor). Although antisense nucleic acids targeted to NF-HEV were known to be effective in ameliorating inflammatory symptoms at the time of the invention, there is no evidence or prior art of record that a polyclonal or monoclonal antibody or a peptide raised against NF-HEV or a ribozyme or an siRNA targeted to the NF-HEV mRNA would result in the claimed therapeutic effect in a subject having an inflammatory condition. Since one of ordinary skill in the art would not know which type of NF-HEV inhibitor other than an antisense nucleic acid complementary to a fragment of NF-HEV would predictably and successfully ameliorate symptoms of an inflammatory condition in a subject, due to the lack of proper guidance and useful teachings in the specification and the prior art, undue experimentation would have been

necessitated for the skilled artisan to practice the entire scope of the claimed therapeutic methods at the time the invention was made.

In view of the foregoing, it is concluded that the specification fails to provide adequate description commensurate in scope with the claimed invention, and therefore, the claims are enabled only insofar as a method of ameliorating symptoms of an inflammatory condition in a subject by reducing the level of NF-HEV comprising administering a single-stranded antisense nucleic acid targeted to a fragment of the NF-HEV mRNA.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 23-25 and 28-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Ruben et al. (WO 99/38881).

The claims are drawn to methods for ameliorating a symptom of a condition associated with inflammation in a subject wherein the methods comprise the step of reducing a nucleic acid encoding a fragment of NF-HEV by administering an antisense nucleic acid complementary to at

least a portion of said nucleic acid (SEQ ID NO:1) encoding a fragment NF-HEV (SEQ ID NO:4).

Ruben et al. teach "Gene No:25" (identified as SEQ ID NO:35), wherein nucleotides 6-1770 of the cDNA sequence are 99.5 % identical to nucleotides 880-2645 of SEQ ID NO:1 of the instant application. Note that SEQ ID NO:1 encodes NF-HEV polypeptide identified as SEQ ID NO:4. They teach that polynucleotides and polypeptides associated with "Gene No:25", such as an antisense nucleic acid, is useful for treating various inflammatory conditions such as ulceretic disorders and wound healing and autoimmune disorders. See pages 51-52, 135, 155, 164-165, 168-171, 235-238, and claim 17. Since Ruben et al. teach the active step of administering an antisense nucleic acid complementary to a fragment of SEQ ID NO:1 of the instant application, which results in amelioration and treatment of inflammatory conditions in a subject, the method of Ruben et al. will inherently result in the reduction of a nucleic acid encoding a fragment of NF-HEV in the subject, absent evidence to the contrary. Accordingly, the claimed invention is anticipated by Ruben et al.

Claims 23-25 and 28-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Jiang et al. (US 2003/0087818 A1).

The claims are described above.

Jiang et al. teach SEQ ID NO:437, wherein nucleotides 65-707 are 97.4% complementary to a nucleotide sequence encoding a fragment of NF-HEV, which corresponds to nucleotides 1995-2645 of SEQ ID NO:1. They teach that the polynucleotide of SEQ ID NO:437 and variants thereof can be formulated as a therapeutic composition for treatment of a condition

associated with inflammation. See paragraphs 1221-1230, 1338-1343, 1395-1405. Since Jiang et al. teach the active step of administering an antisense nucleic acid complementary to a fragment of SEQ ID NO:1 of the instant application, which results in the treatment of condition associated with inflammation in a subject, the method of Jiang et al. will inherently result in the reduction of a nucleic acid encoding a fragment of NF-HEV in the subject, absent evidence to the contrary. Accordingly, the claimed invention is anticipated by Jiang et al.

Claims 23-25, 28-31, and 127 are rejected under 35 U.S.C. 102(e) as being anticipated by Woolf et al. (US 2007/0015145 A1).

The claims are drawn to methods for ameliorating a symptom of a condition associated with inflammation in a subject wherein the methods comprise the step of reducing a nucleic acid encoding a fragment of NF-HEV by administering an antisense nucleic acid complementary to at least a portion of said nucleic acid (SEQ ID NO:1) encoding a fragment NF-HEV (SEQ ID NO:4), wherein the fragment comprises amino acids 1-65 of SEQ ID NO:4.

Woolf et al. teach SEQ ID NO:11450, whose sequence is identical to the entire 2645 nucleotides of SEQ ID NO:1 encoding amino acids 1-270 of NF-HEV polypeptide of SEQ ID NO:4. They teach that an antisense compound targeted to SEQ ID NO:11450 or any therapeutic agent which modulates the activity of the polypeptide encoded by SEQ DI NO:11450 is useful in ameliorating pain induced by inflammation. See paragraphs 0066, 0068, 0417. Accordingly, all claim limitations are taught by Woolf et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23-25, 28-31, and 127 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kasuya et al. (*Acta Neurochirurgica Supplement,* 2001, 77:13-16) in view of Orr et al. (*Current Opinion in Molecular Therapeutics,* 2000, 2:325-331).

The claims are drawn to methods for ameliorating a symptom of a condition associated with inflammation in a subject wherein the methods comprise the step of reducing a nucleic acid encoding a fragment of NF-HEV by administering an antisense nucleic acid complementary to at least a portion of said nucleic acid (SEQ ID NO:1) encoding a fragment NF-HEV (SEQ ID NO:4), wherein the fragment comprises amino acids 1-65 of SEQ ID NO:4, wherein the antisense nucleic acid reduces a pro-inflammatory chemokine.

Kasuya et al. teach a newly discovered novel gene, which they named "DVS27" encodes a nuclear protein involved in inflammatory events and is highly up-regulated in response to inflammatory stimuli, wherein the mRNA as well as protein sequences of the novel gene named "DVS27"which was originally discovered, isolated, and characterized by Kasuya et al. were publicly available as of March 10, 1999 via the NCBI database. See below. Furthermore, it is found that both the mRNA and the protein sequences of "DVS27" of Kasuya et al. are identical to those of "NF-HEV" of the instant application, which are represented by SEQ ID NO:1 and SEQ ID NO:4, respectively. Kasuya et al. do not teach inhibiting "DSV27" by an antisense mechanism to ameliorate an inflammatory condition.

Orr et al. teach that antisense oligonucleotides are effective anti-inflammatory agents and that three patents have been issued for antisense-mediated therapeutics as of the year of 2000, wherein the antisense oligonucleotides reduce cytokine production. See pages 326-327.

```
AB024518
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DEFINITION  Homo sapiens mRNA for DVS27-related protein, complete cds.
ACCESSION   AB024518
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  ORGANISM  Homo sapiens
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            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1
  AUTHORS   Onda,H., Kasuya,H. and Takeda,J.
  TITLE     Identification of genes differentially expressed in canine
            vasospastic cerebral arteries after subarachnoid hemorrhage
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 2645)
  AUTHORS   Takeda,J. and Onda,H.
  TITLE     Direct Submission
  JOURNAL   Submitted (02-MAR-1999) Jun Takeda, Gunma University,Institute for
            Molecular and Cellular Regulation, Laboratory of Molecular
            Genetics,Department of Cell Biology; 3-39-15,Showa-machi, Maebashi,
            Gunma 371-8512, Japan (E-mail:jtakeda@bkaagi.sb.gunma-u.ac.jp,
            Tel:81-27-220-8590, Fax:81-27-220-8558)
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ORIGIN
```

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Qy          1 CACAAGAATACTGAAAAATGAAGCCTAAAATGAAGTATTCAACCAACAAAATTTCCACAG 60
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Qy         61 CAAAGTGGAAGAACACAGCAAGCAAAGCCTTGTGTTTCAAGCTGGGAAAATCCCAACAGA 120
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Qy        181 AGGAGGCCGTTACTTTAGGAGAGAAACCAGCAAAAGGCCTCACTGAAAACAGGTAGAA 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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```

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an antisense agent against "DVS27" of Kasuya et al. and use it to ameliorate an inflammatory condition of a subject.

One of ordinary skill in the art would have been motivated to do so because Kasuya et al. taught that "DVS27" is a novel gene whose protein functions in inflammatory events and whose expression is up-regulated in response to inflammatory stimuli, and therefore the skilled artisan would have wanted to verify whether inhibition of "DVS27" would inhibit inflammatory events by employing the antisense technology known in the art as taught by Orr et al. Furthermore, since various anti-inflammatory antisense oligonucleotides were known to reduce the production level of pro-inflammatory chemokines or cytokines, one of ordinary skill in the art would have had a reasonable expectation of success in reducing the level of pro-inflammatory chemokine in a subject who has been administered an antisense oligonucleotide targeted to the "CVS27" mRNA sequence which encodes a 270-long amino acid protein, thereby ameliorating an inflammatory condition in the subject. Since knowledge and skills required to arrive at the claimed invention were within the technical grasp of one of ordinary skill in the art at the time of the invention, and since the combination of the prior art teachings is as descriptive as the disclosure of the specification, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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